

# Profound Hypothermia in Man \*

## Report of a Case \*\*

SUAD A. NIAZI, M.B., CH.B., F. JOHN LEWIS, M.D. †

*Department of Surgery, University of Minnesota and Ancker Hospital,  
Saint Paul, Minnesota*

### Introduction

Numerous cases of accidental hypothermia resulting from exposure of man to cold have been recorded. Recovery from rectal temperatures of 24 to 30° C. (75 to 86° F.) has been reported by many observers, and Laufman reported recovery from a rectal temperature of 18° C. (64° F.), which was the lowest recorded body temperature reached accidentally by man with survival.<sup>1</sup>

Intentional hypothermia at levels between 25 and 30° C. (77–86° F.) has become relatively popular for cardiac surgery during the last few years since it allows total circulatory interruption for a long enough time to do certain operations within the open heart. There has been no interest in the clinical use of body temperature below 20° C. (68° F.), however. Cooling to these levels was considered to be highly dangerous for warm blooded animals and temperatures below 15° C. (59° F.) were thought to be fatal. Now, after a series of experiments, we have convinced ourselves, despite this earlier opinion, that homeothermic animals can withstand body temperatures much below 15° C. and as low as 0° C. for short periods of time with complete recovery.<sup>2-4</sup> We also found, to our surprise, that the highest animal we tested, the monkey, underwent this profound cooling

with comparative ease.<sup>5</sup> It withstood the cooling much better than the dog did, for example. The success with which this primate tolerated profound cooling plus some observations on the fate of experimental cancer during cooling led us to cool the patient whose case we reported here. These observations in experimental cancer concerned the regression of transplanted cancers in rats cooled to temperatures near freezing. We found that actively growing, transplanted, malignant tumors regressed completely in most of a small series of rats cooled to near freezing temperatures.<sup>6</sup> Our employment of profound cooling to treat cancer is, of course, preceded by the extensive trials of moderate hypothermia in this role in the early 1940's which were stimulated by the work of Temple Fay.<sup>7</sup>

In this report we will describe how the body temperature of a 51-year-old woman, with a terminal cancer of the ovary, was lowered temporarily to 9° C. with survival. This patient reached the low temperature in a state of cardiac and respiratory standstill which lasted for a period of one hour.

### Method

The technic of cooling was similar to the technic we have used for the animals.<sup>2-6</sup> Surface cooling was achieved by wrapping the patient in rubberized blankets through which a refrigerant circulated at -1° C. to -7° C. The body temperature was measured rectally by a mercury thermometer and also by an electrical thermometer. An endotracheal tube was inserted and an

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† Now of the Department of Surgery, Northwestern University Medical School, Chicago.

intermittent positive pressure, artificial respirator was used during cooling. The respirator employed a semi-open system and a gas mixture consisting of 5 per cent CO<sub>2</sub> and 95 per cent oxygen was used. The respiratory pressure of the inhaled gas was 18 to 20 mm. of mercury and the minute respiratory volume was 8 to 11 liters. Respiratory rate was 10 to 13 per minute and the expiratory and inspiratory cycles were equal. Respiration was discontinued during the period of cardiac standstill.

Sodium pentothal was administered for anesthesia as a 2.5 per cent solution in distilled water and 80 mgm. of gallamine triethiodide (Flaxedil®) were added to each 20 milliliters of this solution before injection. The total dose of pentothal given was 1.525 grams. No anesthetic was used during rewarming. The heart action was watched electrocardiographically on both an oscilloscope and a direct writing machine during the experiment and the intra-arterial blood pressure was measured by a mercury manometer connected to the radial artery through a polyethylene tube.

Rewarming was achieved, as in the experimental animals, by using wet packs at 45° C. which were applied to the chest until the heart resumed beating following which the whole body was warmed in the same manner. Warming in a water bath at 45° C. was used later as the body temperature reached 20° C.

### Case Report

A 51-year-old woman (A. H. #211243) who weighed 95 pounds was admitted to the hospital on December 19, 1955, as a terminal case of ovarian cancer. She had first noticed ill health in February 1955, eleven months prior to the December admission. An abdominal exploration in June 1955 had revealed a carcinoma of the ovary with extensive intra-abdominal metastases. In December 1955, she had numerous large pelvic and intra-abdominal masses and bilateral pulmonary metastases. When we were first called in consultation she had a complete small bowel obstruction caused by her metastases. This obstruction was partially relieved with long-tube suction, and the

possibility of trying profound hypothermia as a treatment for her malignancy was presented to her.

She accepted, and on December 28, 1955, she was cooled. The heart rate gradually decreased from 100 per minute at 37° C. to 4 per minute at a body temperature of 11.2° C. and it continued at this rate for 34 minutes before the beat finally ceased, as planned, at 10.5° C. The P-wave of the electrocardiogram disappeared at 13° C. and a slow idioventricular rhythm continued until cardiac standstill occurred. The QRS complexes were very wide before cardiac standstill took place and the S-T segment was displaced. The T-wave varied in height and occasionally they were depressed or biphasic at temperature levels below 20° C. The lowest body temperature reached was 9° C.

After cardiac standstill had continued for 45 minutes, rewarming was commenced and the heart beat returned at a rectal temperature of 10° C. Cardiac standstill had lasted for one hour. The beat was slow and irregular, and the QRS complexes were very wide. The P-wave returned at 12° C., 30 minutes after the return of ventricular beats, and the heart rate increased gradually until it was 100 per minute when the temperature had reached 36° C.

Arterial blood pressure dropped gradually during cooling from 130 mm. of mercury systolic at 37° C. to 12–16 mm. at 11° C. to 13° C., when the heart rate was 4 to 8 per minute. The blood pressure recorded during cardiac standstill was less than 10 mm. of mercury.

The changes in blood pH, plasma carbon dioxide and serum potassium and sodium are shown in Table I.

The patient recovered consciousness 10 hours after regaining normal body temperature. Her mental condition and intelligence were apparently not changed. She remembered our names immediately after recovery and inquired about the lowest temperature she attained.

She remained pleasant and alert for one week after cooling and then became confused and dis-

TABLE I. *Blood Changes During Cooling and Rewarming*

| Temp.<br>°C. | pH   | Plasma CO <sub>2</sub><br>mM/L | Na<br>mEq/L | K<br>mEq/L |
|--------------|------|--------------------------------|-------------|------------|
| 38           | 7.32 | 24.7                           | 140.0       | 6.34       |
| 29.5         | 7.36 |                                |             |            |
| 23           | 7.38 | 25.96                          | 152.6       | 3.45       |
| 18.5         | 7.40 |                                |             |            |
| 14           | 7.40 | 26.51                          | 155.64      | 4.14       |
| 12           | 7.45 | 24.01                          | 133.91      | 5.78       |
| 36           | 7.47 | 18.96                          | 108.68      | 4.22       |

oriented for several days. This may have been due to dehydration as her fluid intake had been unusually low for a number of days (150–200 cc. per day). This state of confusion disappeared when her dehydration was corrected by intravenous fluids.

The patient lived 38 days after cooling and died following 2 days of fever and oliguria. At autopsy she was found to have widespread metastases. The terminal episode was apparently caused by malignant ureteral obstruction and pyonephrosis. Though there was some necrosis in her tumor, both grossly and microscopically, there was no clear-cut evidence that the tumor had been damaged by cooling.

### Discussion

It is evident that a number of homeothermic animals, including man, can tolerate cooling to body temperatures near freezing—temperatures attained regularly by true hibernators. Unlike the hibernators, however, the warm-blooded animals are brought through the lower temperature ranges in a state of cardiac standstill which may usually last up to two and one-half hours, though as long as four hours has been tolerated in the rat (one hour in the patient reported here). In the hibernators the heart continues to beat at a slow rate even at the low temperatures.

This unexpected ability of warm-blooded animals to survive low temperatures without harm brings us to speculate on the possibilities of achieving still lower temperatures. If the freezing point could be safely passed, presumably some degree of suspended animation could actually be reached. Individual cells such as spermatozoa can survive cooling to  $-70^{\circ}\text{C}$ . and long periods of storage.<sup>8</sup> May this be possible with the intact animal? As yet we have made little progress in this direction though some of our rats have survived cooling (apparently supercooling) to  $-4^{\circ}\text{C}$ . Smith<sup>9</sup>

working with the golden hamster, a hibernator, has revived animals from a partially frozen state.

### Summary

In a 51-year-old woman widespread, metastatic ovarian carcinoma was treated by body cooling to a rectal temperature of  $9^{\circ}\text{C}$ . ( $48^{\circ}\text{F}$ .). This low temperature was reached, as planned, during cardiac standstill which lasted for one hour, yet the immediate recovery was complete. Unfortunately, her cancer did not regress, and she succumbed to the disease 38 days after the cooling.

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